

Concurrent central nervous system infective pathology in a severely immunocompromised patient

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ABSTRACT

To our knowledge and literature search, concurrent cryptococcal meningitis and neurosyphilis in a patient have rarely been reported. Here, we report a 37-year-old male with HIV infection presented with headache and dizziness for 5 days along with memory difficulty and personality changes for about 1 week. During the hospital stay, cryptococcal meningitis was confirmed with positive cerebral spinal fluid (CSF) cryptococcal antigen titer (1:320) and positive CSF culture. Diagnosis of neurosyphilis was made based upon CSF white blood cell count of 85 cells/ μ L, with CSF total protein of 87 mg/dL, reactive CSF treponemal antibody, and fluorescent treponemal antibody. The patient was treated with amphotericin B, flucytosine, fluconazole, and benzathine penicillin G, and the patient was recovered and discharged. HIV patients are at high risk of developing severe infections of the central nervous system. Awareness should be made not only to single infection but also for dual pathology for a better and life-saving management.

Keywords: Central nervous system infection, cryptococcal meningitis, human immunodeficiency virus, neurosyphilis

Introduction

The most common infectious agents causing meningeal illnesses in patients with HIV include *Cryptococcus neoformans* and *Mycobacterium tuberculosis*. Syphilitic involvement by *Treponema pallidum* however is rare and the coexistence of an underlying HIV disease may add a more rapid disease progression. Cryptococcal meningitis, especially in HIV-infected patients, frequently results in relatively minor cerebral spinal fluid (CSF) changes. However, higher than expected protein and cell count in CSF could indicate coinfection.

Case Report

A 37-year-old male with the past medical history of HIV infection presented to the emergency department with complaints of headache, dizziness for 5 days along with memory difficulty and personality change for about 1 week. The patient experienced bitemporal headache intermittently for 5 days with intensity of

eight out of 10. According to the patient, the headache was aching in nature, nonradiating, and without aggravating or relieving factors. It was associated with dizziness and photophobia. However, he denied fever, nausea, vomiting, numbness of the extremities, dyspnea, skin rash, fever, myalgia, joint pains, oral ulcers, soreness in his lip, genital discharge, or any genital lesion. The patient had an established diagnosis of HIV 10 years ago and his last cluster of differentiation-4 (CD4) cell count of 300 and ribonucleic acid (RNA) viral load (VL) 15,000 4 years ago and not compliant with highly active antiretroviral therapy (HAART). He is allergic to penicillin-causing hives. The patient stated to be sexually active with his boyfriend but did not use condoms during sexual intercourse.

Initial vital signs included temperature 98.3°F, pulse rate 123 beats/min, respiratory rate 20 breaths/min, blood pressure 116/86 mmHg, and oxygen saturation 97% on room air.

Physical examination revealed normal motor 5/5 in power, intact sensation, normal vibration and position sense, normal

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coordination, negative cerebellar signs, hyporeflexia (1+) in all four limbs, Babinski sign was downgoing, negative asterixis in all four limbs, and normal gait. The patient had poor short-term memory and recent personality change causing him irritable sometimes. He exhibited nuchal rigidity with positive Kernig's sign (when the thigh was bent at the hip and knee at 90° angles, subsequent extension in the knee is painful). The patient had photophobia but negative Brudzinski's sign or focal neurological deficit. Vision and hearing were otherwise normal. Pupils were equal, normal, and reactive to light. Pulmonary, cardiovascular, and abdominal examinations were within normal limits.

Initial laboratory tests showed white blood cells (WBCs) $6.2 \times 10^9/L$, neutrophil percentage (auto) 85.8%, neutrophils (auto) 5.3 K/ μL , lymphocytes percentage (auto) 7.3%, lymphocytes (auto) 0.5 K/ μL , normal sodium and potassium levels, blood urea nitrogen 4 mg/dL, creatinine 0.5 mg/dL, glucose 118 mg/dL, calcium 9.7 mg/dL, aspartate aminotransferase 31 IU/L, total bilirubin 0.7 mg/dL, alanine aminotransferase 56 IU/L, and alkaline phosphatase 90 IU/L. Immunologic tests revealed percent CD4 cells 0.9%, absolute CD4 count 6 cells/ μL , percent CD3 cells 66.3%, absolute CD3 count 418 cells/ μL , T-lymphocyte CD4/CD8 ratio 0.02 (normal 0.6–4.4), normal CD19, and normal CD8 count. Other blood tests showed HIV fourth-generation test positive, HIV RNA polymerase chain reaction (PCR) 263994, HIV RNA PCR log 10 value 5.42 (normal < 1.3), serum cryptococcal antigen (CrAg) positive with antigen titer 1:160, herpes virus one and two DNA PCR negative, *Mycobacterium* complex PCR negative, and cytomegalovirus DNA PCR negative. Patient's serum rapid plasma reagin test was positive along with positive serum fluorescent treponemal antibody absorption (FTA-ABS) test. Blood cultures were negative and urinalysis showed normal urine. Chest X-ray and head computed tomography (CT) were unremarkable.

Patient underwent lumbar puncture (LP) procedure which showed opening pressure 290 mm H₂O, with clear and colorless CSF, WBC 85 cells/ μL , neutrophils 8 cells/ μL , lymphocytes 85 cells/ μL , red blood cell 0 cells/ μL , monocytes 6 cells/ μL , eosinophils 1 cells/ μL , basophils 0 cells/ μL , chloride 122 mmol/L, glucose 40 mg/dL, total protein 87 mg/dL, CSF venereal disease research laboratory (VDRL) nonreactive, CSF FTA reactive, CSF CrAg-positive with titer 1:640, CSF cryptococcal culture-positive, and CSF cytomegalovirus and toxoplasma virus antigen negative.

Since the patient had penicillin allergy, penicillin desensitization was performed in the Intensive Care Unit and benzathine penicillin G 3 million units intravenous every 4 h for 14 days was given for neurosyphilis. Moreover, 2 weeks of amphotericin B lipid complex 350 mg IV daily and flucytosine 1500 mg per os every 6 h were administered for induction therapy of cryptococcal meningitis. The patient was also given acetaminophen 650 mg per os and diphenhydramine 50 mg per os were given to prevent infusion reaction. Two weeks later, a repeat LP demonstrated opening pressure 200 mm H₂O, negative CSF cryptococcal

culture. Amphotericin B and flucytosine were stopped and fluconazole 400 mg per os daily was started. Benzathine penicillin 2.4 million units was given intramuscularly and to be administered for total of 3 weeks for late latent syphilis. Dapsone 100 mg per os daily and azithromycin 1,200 mg per os every week were given for prophylaxis of opportunistic infections in immunocompromised state. Abacavir 600 mg per os daily, dolutegravir 50 mg per os daily, and lamivudine 300 mg per os daily combination was started as a HAART regimen. Over the course of his hospital stay, the patient's initial symptoms of headache and dizziness subsided. He was then discharged from the hospital. Nine months later, in a follow-up visit to the HIV clinic, patient's blood tests revealed CD4 count of 85 cells/ μL , HIV RNA VL (PCR) of 51, and HIV RNA PCR log 10 value of 1.71. The patient was apparently in good health without any headache, memory loss, personality change, or neurological deficits.

Discussion

LP is the diagnostic procedure of choice for cryptococcal meningitis which mostly showed a low WBC count in the CSF (e.g., <50 cells/ μL) with a mononuclear predominance.^[1] CSF protein may be mildly elevated while the glucose concentrations are usually low. Nearly, 25% of patients with culture-positive cryptococcal meningoencephalitis have a normal CSF profile.^[2–4] A positive CrAg in the CSF indicates the diagnosis of cryptococcal meningitis and can initiate treatment in patients with symptoms. An LP should be repeated for fungal culture after 2 weeks of induction therapy to confirm sterilization of the CSF.

The diagnostic analysis of CSF for neurosyphilis includes a mononuclear, predominant pleocytosis >10 cells/ μL , elevated protein concentration >45 mg/dL, and normal or decreased glucose concentration. Although CSF-VDRL tests may be abnormal in syphilitic meningitis (70–80% sensitivity), a negative result does not rule out neurosyphilis.^[5] In some cases, initial CSF-VDRL may be negative. On the other hand, CSF FTA-ABS test is less specific but more sensitive than CSF-VDRL and may be used to exclude the neurosyphilis. In addition, PCR assays detect *T. pallidum* in CSF 50% of patients for syphilitic CNS involvement. During HIV coinfection, mild to moderate CSF pleocytosis is detected along with elevated protein levels.^[5–7] Diagnosis of neurosyphilis is based on clinical judgment and patient immune status. In HIV patients, LP is recommended if serological tests for syphilis are positive and in the presence of neurological symptoms. Although CSF-VDRL is negative in our case, CSF WBC and protein were high enough (supported by CSF FTA test reactive test) to start treatment for neurosyphilis.^[8,9]

Conclusion

Cryptococcal meningitis alone in HIV-infected patients often results in relatively minor CSF changes; however, coinfection with neurosyphilis will lead to elevated proteins and cell counts to a higher than expected level. Empiric treatment with penicillin for neurosyphilis should be started as soon as LP abnormalities

are consistent with neurosyphilis and presence of neurological symptoms.

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Conflicts of interest

There are no conflicts of interest.

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